



Research Article

The relationship between maternal vitamin D status during third trimester of pregnancy and maternal and neonatal outcomes: A longitudinal study

Mahboobeh Shakeri¹ M.Sc., Sima Jafarirad^{2,3} Ph.D.

¹Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

²Nutrition and Metabolic Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

³Department of Nutrition, School of Para-medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract

Background: Vitamin D deficiency is a common nutritional concern and leads to several problems among some population groups.

Objective: The aim of the current study was to evaluate the relationship between maternal vitamin D status and gestational weight gain, maternal biochemical parameters, mode of delivery, and infants' growth indices at birth.

Materials and Methods: A longitudinal study between March and June 2017 was carried on 82 mothers in Ahvaz. Blood samples of each mother were obtained at the mean of the third trimester to assay lipid indices (total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein cholesterol), fasting blood sugar, and 25-hydroxy vitamin D. Anthropometric assessment of newborns was recorded from neonatal health card at birth.

Results: Mean maternal 25-hydroxy vitamin D level was 22.52 nmol/L; 7.33% of mothers had vitamin D deficiency, 76.6% had vitamin D insufficiency, and 15.9% were normal. The mean neonate birth weight, length, and head circumference of mothers who were on the third tercile of 25-hydroxy vitamin D serum level was significantly higher than those in the first tercile ($p < 0.001$, $p = 0.004$ and $p < 0.001$, respectively). Maternal vitamin D serum level had an adverse relationship with fasting blood sugar.

Conclusion: Low levels of serum vitamin D may cause adverse pregnancy outcomes and delivery of infants with insufficient growth at birth.

Key words: Vitamin D, Pregnancy, Infant, Growth, Delivery, Blood glucose.

Corresponding Author:

Sima Jafarirad;

email: Jafarirad-s@ajums.ac.ir

sjafarirad@gmail.com

Postal Code: 61357-15794

Tel: +989112527976

Received 27 December 2017

Revised 20 June 2018

Accepted 12 September 2018

Production and Hosting by
Knowledge E

© Mahboobeh Shakeri and Sima Jafarirad. This article is distributed under the terms of the [Creative Commons](#)

[Attribution License](#), which permits unrestricted use and redistribution provided that the original author and source are credited.

Editor-in-Chief:

Aflatoonian Abbas M.D.



OPEN ACCESS

1. Introduction

Vitamin D is a key nutritional factor for maternal and infants' health. The fetus level of vitamin D is totally dependent on their mother's levels of 25-hydroxy vitamin D (25(OH)-D). The circulating levels of 25(OH)-D is the marker to represent vitamin D status. It correlates with the intake of vitamin or sun exposure during pregnancy (1). Vitamin D has a key role in fetal growth by regulating the parathyroid hormone and increasing calcium absorption. The complication of low consumption of calcium status or insufficient vitamin D is high secretion of parathyroid hormone (2).

Vitamin D deficiency is common in pregnant women which affects not only the mothers' health but also of the infants (3). The deficiency probably causes a weak growth of fetal during pregnancy. Some studies have emphasized on post- and post-delivery effects of vitamin D on weak bone mineralization of infants that has an important relationship with short growth age (4).

Low maternal vitamin D level has been linked with preeclampsia, gestational diabetes, postpartum depression, and stillbirth (5). Furthermore, vitamin D insufficiency in uterus or early stages of life increases the risk of several diseases such as childhood wheezing, respiratory infection, and type 1 diabetes mellitus (6). So normal vitamin D level is necessary during pregnancy, and recognition of risk factors and primary diagnosis of vitamin D status during pregnancy is essential to prevent deficiency and its complications (4).

Mothers' weight can affect vitamin D serum levels. One study showed that the mean serum level of 25(OH)-D in pregnant women with pre-pregnancy overweight [body mass index (BMI)=25-29.9] was more than that of pregnant women with normal pre-pregnancy BMI (BMI=18.5-24.9) (7), while other studies confirmed that obese mothers had low levels of 25(OH)-D (8).

Ahvaz is a city located in the south west of Iran with mostly sunny days, but it seems that in Iran, the clothing style and lack of seasonal foods can affect vitamin D status in women . This study was done to evaluate the vitamin D status among pregnant women residing in this city. Since there were few studies about the linkage of maternal vitamin D serum level with pre-pregnancy BMI, gestational weight gain, maternal blood sugars, lipid profiles as well as anthropometric measurements of neonates, the present study was aimed to find the association between maternal vitamin D status during third trimester and gestational weight gain, maternal blood sugar, lipid profiles, mode of delivery, and infant's weight, length, and head circumference at birth.

2. Materials and Methods

2.1. Subjects' recruitment

This study was a longitudinal and cross-sectional survey and conducted on pregnant women living in Ahvaz (a city in the south west of Iran) between March and June 2017. Subjects recruited were healthy pregnant women referred to two health centers' representatives of the East and the West of Ahvaz. The inclusion criteria included age range 18–45 yr at the expected date of delivery and women who were during the third trimester of pregnancy. Those having chronic infectious diseases, metabolic disorders, gestational diabetes, gestational hypertension, preeclampsia, eclampsia, twin pregnancy, eating disorders (anorexia, bulimia), emotional disorders (depression, stress, and anxiety), drug consumption, and taking multi-vitamin supplements (out of health centers routine programs) were excluded. Applying the inclusion and exclusion criteria, 88 pregnant women were selected.

2.2. Data gathering

A demographic questionnaire including personal information (age, education, job, ethnic). In addition, disease history was investigated. Gestational weight gain was assessed from the data of the pregnant women recorded files. The trimesters were defined as first (less than 14 completed wk), second (14–27 completed wk), and third (28 completed wk until delivery). Weight gain during the third trimester was estimated using the difference between the first and last weight recorded divided by the number of weeks between the two visits (9). Three days food recall (two work days and one holiday) questionnaire was completed for all subjects to determine micro- and macro-nutrients intake.

Weight and height of mothers were determined with an accuracy of 0.1 kg and 0.1 cm, respectively. BMI was calculated using this formula: $\text{bodyweight}/(\text{height})^2$; in this formula bodyweight is presented as kilogram and height as meter. An appropriate weight gain was recommended by the institute of Medicine and National Research Council guideline based on pre-pregnancy BMI. Those in the underweight (BMI<18.5) category were recommended to aim at gaining 12.5–18 kg, normal (BMI=18.5–24.9) 11.5–16 kg, overweight (BMI=25–29.9) 7–11.5 kg, and obese (BMI>30) 5–9 kg (9).

For measuring vitamin D, 5 ml of venous blood were obtained from each mother at the mean of third trimester to assay 25(OH)-D level using the enzyme-linked immunosorbent assay (ELISA, EUROIMMUN, Germany). Tercile of serum vitamin D were determined to evaluate the mothers' vitamin D status.

Fasting blood sugar (FBS) and lipid profiles (triglyceride, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), and total cholesterol were determined using an auto-analyzer (Hitachi 911, Japan).

After delivery, the infant's growth indices at birth (including weight, height, and head circumference) were collected from their health cases in health centers.

2.3. Ethical consideration

The study was approved by the Ethics Committee of the Ahvaz Jundishapur University of Medical Sciences (IR.AJUMS.REC.1395.837). All subjects completed an informed consent form.

2.4. Statistical analysis

Statistical analysis was performed using SPSS software (Statistical Package for the Social Sciences, version 17.0, SPSS Inc. Chicago, USA). Data were expressed as means \pm standard deviations (SD) for continuous variables or number (percentage) for categorical variables. One-way analysis of variance (ANOVA) was used to analyze the difference of each variable among mothers with different vitamin D status. Tukey post-hoc analysis was done to confirm the significant difference of variables among groups of mothers with different vitamin D status. Odds ratio (OR) was determined to measure if vitamin D insufficiency could predict the probability of low weight, length, and head circumference at birth. p -value < 0.05 was considered as significant level.

3. Results

From 88 pregnant women, 82 subjects delivered healthy and term neonates; hence, 82 women were included in the analysis. The characteristics of these women are described in Table I.

3.1. Demographic data

53.6% of women were between 18–30 yr and 46.3% women were >30 yr. According to the

BMI levels before pregnancy, mothers were categorized as underweight: (2.4%), normal weight: (56.1%), overweight: (31.7%), and obese: (9.8%). The number in each group for total weight gain that was categorized as insufficient, adequate, and excessive were 15(18.3%), 39(47.6%), and 28(34.1%) women, respectively. None of the subjects followed a special diet.

3.2. Maternal 25-hydroxy vitamin D serum level

Of all mothers, 7.33% had vitamin D deficiency, 76.6% insufficiency, and 15.9% were in normal range. Also, mothers were categorized based on the tercile of 25(OH)-D serum levels to first, second, and third tercile.

Analysis revealed that the birth weight of infants who were born by mothers in the first tercile of 25(OH)-D serum level was significantly lower than that of the second and third tercile ($p < 0.001$). Moreover, women in the first tercile had

shorter infants compared to women in the third tercile of vitamin D serum levels ($p = 0.004$) (Table II). The OR confirmed that vitamin D deficiency and insufficiency could predict 1.3 and 1.32 times lower birth weight (LBW) and lower infants' length at birth, respectively (Table III). ANOVA indicated significant difference between maternal vitamin D status and neonates' head circumference (Table II). Also, vitamin D deficiency and insufficiency could predict 1.29 times infants with head circumference (HC) under 25th percentile (Table III).

Data also revealed that mothers who delivered babies via cesarean sections had significantly less vitamin D serum level compared to mothers who experienced natural vaginal delivery ($p = 0.027$) (Figure 1).

There was no relationship between maternal vitamin D status and gestational weight gain and serum lipid profiles (total cholesterol, triglyceride, LDL-C, and HDL-C), but mothers in the first tercile of vitamin D status had more FBS than those in the third tercile; however, it was in the normal range (Table II).

Table I: General data of pregnant subjects.

Variable (N = 82)	
Maternal age (yr)*	29.8 ± 5.45
Total weight gain (kg)*	13.80 ± 4.22
Maternal vitamin D serum level (nmol/L)*	22.52 ± 15.99
Birth weight (g)*	2990 ± 430
Height (cm)*	48 ± 3.57
Head circumference (cm)*	34.05 ± 1.13
Fasting blood sugar (mg/dL)*	76.51 ± 8.02
Total cholesterol (mg/dL)*	238.93 ± 43.93
High density lipoprotein (mg/dL)*	58.97 ± 10.59
Low density lipoprotein (mg/dL)*	138.70 ± 35.00
Triglyceride (mg/dL)*	203.04 ± 70.66
Education**	
Diploma and lower education	43 (52.4)
Academic education	39 (47.6)
Ethnicity **	
Turk and Kurd	3 (3.65)
Lor	23 (28)
Persian	12 (14.6)
Arab	44 (53.6)

Note: * Data presented as mean ± SD. ** Data presented as n (%).

Table II: The differences between maternal weight gain and biochemical parameters during pregnancy and neonates' anthropometric indices at birth among mothers in different tercile groups of 25-hydroxy vitamin D serum level.

	Maternal Vitamin D Status			p-value*
	First tercile	Second tercile	Third tercile	
Neonate anthropometric measurements				
Birth weight (g)	2200 (121) ^a	2970 (351) ^b	3491 (220) ^b	< 0.001
Birth length (cm)	43.75 (0.88) ^a	47.63 (2.41) ^{ab}	51.76 (5.53) ^b	0.004
Birth head circumference (cm)	32.41 (0.37) ^a	34.01 (1.07) ^b	35.00 (0.54) ^b	< 0.001
Maternal weight gain				
Total weight gain	14.83 (4.70)	13.91 (4.30)	12.76 (3.73)	0.56
Biochemical parameters				
FBS (mg/dL)	78.37 (9.10) ^a	78.98 (8.46) ^{ab}	72.35 (4.09) ^b	0.002
T.CHO (mg/dL)	241.85 (45.48)	244.25 (44.18)	231.00 (42.83)	0.34
HDL (mg/dL)	56.25 (10.39)	59.92 (9.39)	60.67 (11.67)	0.5
LDL (mg/dL)	142.48 (38.18)	140.33 (32.92)	133.55 (34.40)	0.11
TG (mg/dL)	203.73 (70.45)	215.74 (81.23)	190.17 (59.27)	0.26

Note: Data presented as mean (SD); Different letters confirm significant differences (Tukey post-hoc analysis); *One way analysis of variances;

FBS: Fasting Blood Sugar; T.CHO: Total cholesterol; HDL: High Density Lipoprotein;

LDL: Low Density Lipoprotein; TG: Triglyceride.

Table III: The OR for low neonate growth indices at birth according to vitamin D status of mothers.

Neonate growth indices at birth		Maternal Vitamin D status				
		Deficient or insufficient	Sufficient	p-value*	OR	95% CI
Birth weight (Percentile)	< 25	26 (100)	0	0.007	1.302	1.128–1.504
	> 25	43 (76.8)	13 (23.26)			
Birth length (Percentile)	< 25	29 (100)	0	0.003	1.325	0.136–1.545
	> 25	40 (75.5)	13 (24.5)			
Birth head circumference (Percentile)	< 25	25 (100)	0	0.008	1.295	1.125–1.492
	> 25	44 (72.2)	13 (28.8)			

Note: Data presented as *n* (%); OR: odds ratio; CI: confidence interval; *Chi-square test.

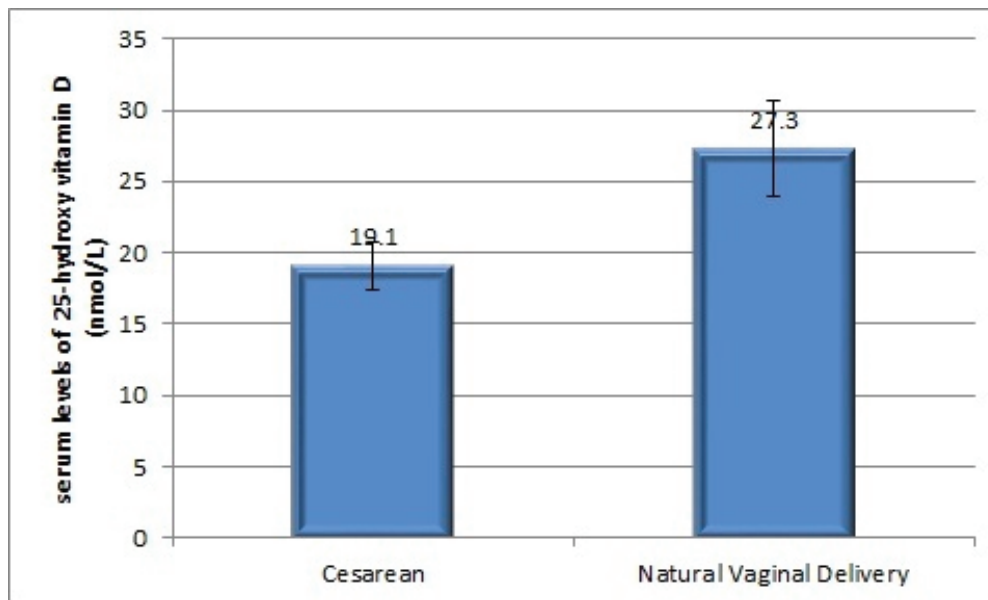


Figure 1: The relationship between vitamin D status of pregnant women and mode of delivery (Chi-square test).

4. Discussion

The present study was performed on pregnant women to find the relationship of maternal vitamin D serum level with weight gain during pregnancy and infants' weight, length, and HC at birth.

4.1. Maternal vitamin D status and infant's growth indices at birth

A significant association was found between maternal lower vitamin D serum levels and LBW, which was compatible with the results of other studies (10–13). One study in Netherlands and another from Australia found significantly LBW among infants born to women with vitamin D deficiency (12, 13). Also Bodnar and colleagues have reported a positive relationship between vitamin D deficiency and neonatal LBW in white mothers and not in black mothers (11). However, other researchers found no association between maternal vitamin D status and normal- or low birth weight (14).

Our finding indicated a significant positive relationship between maternal vitamin D serum levels and neonatal length, which is in line with

the previous research that showed a significant relationship between inadequate vitamin D intake during pregnancy and low neonatal birth weight and shorter infant height (15, 16), while other studies did not find any relationship between maternal vitamin D deficiency and neonatal length (10).

Also, in this study, mothers with vitamin D deficiency or insufficiency delivered neonates with HC ≤ 33 cm, consistent to another study (10). However, inconsistent to our results, another study showed an independent correlation between neonatal HC and maternal vitamin D level (17).

It seems that the effect of vitamin D on growth indices at birth is related to the role of this vitamin in bone mineralization and the following low levels of it lead to less bone growth (4). Consequently, the levels of mothers' serum vitamin D may predict the infants' growth indices at birth.

4.2. Maternal vitamin D status and serum biochemical parameters

Our finding showed that serum levels of 25(OH)-D had significantly inverse correlation with FBS that is in line with another study (18). Also, our

results support previously reported results in which serum concentrations of 25(OH)-D levels during 24–28 wks of gestation were significantly lower in women with gestational diabetes mellitus than in groups with normal levels of vitamin D (19). While our findings found no significant relationship between mothers' vitamin D status and lipid indices (total cholesterol, triglycerides, LDL-C, and HDL-C), another survey that studied 25(OH)-D serum levels among a population of men showed a significant association between low levels of 25(OH)-D and high levels of LDL-C, but no association with HDL-C (20). However, in a study that was performed on Saudi pregnant women, serum vitamin D in the subjects surprisingly correlated positively with the serum levels of triglycerides and cholesterol (21).

Some proposed mechanisms could display the relation between vitamin D deficiency and risk of elevated blood glucose or gestational diabetes mellitus. Protective effects of vitamin D on pancreas beta-cells finally lead to the regulation of insulin secretion (22). Also, some evidence related to vitamin D deficiency with abnormal glucose and dyslipidemia and other epidemiologic studies has revealed that pregnant women with gestational diabetes are more likely to be vitamin D-deficient mothers (19).

4.3. Maternal vitamin D status and mode of delivery

In the present study, a significant difference was found between the mode of delivery and mothers' vitamin D status, which confirms the results of a cross-sectional survey and a clinical trial that both of them show the vitamin D effect on the risk of primary caesarian-section (23, 24). In that cross-sectional study, 25(OH)-D levels < 37.5 nmol/L were associated with four-fold increased odds of requiring first-time (primary) cesarean section (23); while the result of that randomized clinical trial showed no effect of vitamin D supplementation on the mode of delivery (24). Some reasons could be

pointed out to describe this association such as the key role of vitamin D in calcium homeostasis (including an effect on muscle function and may help to starting labor); although, further exploration would be required (25).

The limitation of the study was that it did not evaluate the effect of supplements intake and the amount of sunlight exposure on the vitamin D status. We speculate that these factors should be considered in future studies.

5. Conclusion

This study shows that maternal low 25(OH)-D level could be related to their infant's lower weight, shorter height, and lower HC at birth. Also, it was associated with the mode of delivery. However, serum vitamin D in these subjects did not correlate with the serum levels of triglycerides, cholesterol, LDL-C, and HDL-C, but a significant adverse association was found between FBS and maternal vitamin D levels. So, the findings of this study showed that vitamin D during pregnancy may have ample importance and it can be suggested that vitamin D status screening during pregnancy could help prevent low infant growth indices at birth and undesirable effects on the mothers.

Acknowledgments

The authors greatly appreciate all the pregnant women who participated in the study. Additionally, this study was supported by the Student Research Committee of Ahvaz Jundishapur University of Medical Sciences (95S30).

Conflict of interest

The authors declare that they have no conflicts of interest.

References

- [1] Novakovic B, Galati JC, Chen A, Morley R, Craig JM, Saffery R. Maternal vitamin D predominates over genetic factors in determining neonatal circulating vitamin D concentrations. *Am J Clin Nutr* 2012; 96: 188–195.
- [2] Hatfield DP, Sweeney KP, Lau J, Lichtenstein AH. Critical assessment of high-circulation print newspaper coverage of the Institute of Medicine Report Dietary Reference Intakes for Calcium and Vitamin D. *Public Health Nutr* 2014; 17: 1868–1876.
- [3] Bodnar LM, Simhan HN, Catov JM, Roberts JM, Platt RW, Diesel JC, et al. Maternal vitamin D status and the risk of mild and severe preeclampsia. *Epidemiology* 2014; 25: 207–214.
- [4] Karim SA, Nusrat U, Aziz S. Vitamin D deficiency in pregnant women and their newborns as seen at a tertiary-care center in Karachi, Pakistan. *Int J Gynaecol Obstet* 2011; 112: 59–62.
- [5] Gernand AD, Simhan HN, Klebanoff MA, Bodnar LM. Maternal serum 25-hydroxyvitamin D and measures of newborn and placental weight in a US multicenter cohort study. *J Clin Endocrinol Metab* 2013; 98: 398–404.
- [6] Shin YH, Yu J, Kim KW, Ahn K, Hong SA, Lee E, et al. Association between cord blood 25-hydroxyvitamin D concentrations and respiratory tract infections in the first 6 months of age in a Korean population: a birth cohort study (COCOA). *Korean J Pediatr* 2013; 56: 439–445.
- [7] Pratumvinit B, Wongkrajang P, Wataganara T, Hanyongyuth S, Nimmannit A, Chatsiricharoenkul S, et al. Maternal vitamin D status and its related factors in pregnant women in Bangkok, Thailand. *PLOS ONE* 2015; 6: 10:e0131126.
- [8] Bodnar LM, Catov JM, Roberts JM, Simhan HN. Prepregnancy obesity predicts poor vitamin D status in mothers and their neonates. *J Nutr* 2007; 137: 2437–2442.
- [9] Girard AW, Olude O. Nutrition education and counselling provided during pregnancy: effects on maternal, neonatal and child health outcomes. *Paediatr Perinat Epidemiol* 2012; 26 Suppl 1: 191–204.
- [10] Khalessi N, Kalani M, Araghi M, Farahani Z. The relationship between maternal vitamin D deficiency and low birth weight neonates. *J Family Reprod Health* 2015; 9: 113–117.
- [11] Bodnar LM, Catov JM, Zmuda JM, Cooper ME, Parrott MS, Roberts JM, et al. Maternal serum 25-hydroxyvitamin D concentrations are associated with small-for-gestational age births in white women. *J Nutr* 2010; 140: 999–1006.
- [12] Bowyer L, Catling-Paull C, Diamond T, Homer C, Davis G, Craig ME. Vitamin D, PTH and calcium levels in pregnant women and their neonates. *Clin Endocrinol (Oxf)* 2009; 70: 372–377.
- [13] Leffelaar ER, Vrijkotte TG, van Eijsden M. Maternal early pregnancy vitamin D status in relation to fetal and neonatal growth: results of the multi-ethnic Amsterdam born children and their development cohort. *Br J Nutr* 2010; 104: 108–117.
- [14] Morley R, Carlin JB, Pasco JA, Wark JD, Ponsonby AL. Maternal 25-hydroxyvitamin D concentration and offspring birth size: effect modification by infant VDR genotype. *Eur J Clin Nutr* 2009; 63: 802–804.
- [15] Fernández-Alonso AM, Dionis-Sánchez EC, Chedraui P, González-Salmerón MD, Pérez-López FR, Spanish Vitamin D and Women's Health Research Group. First-trimester maternal serum 25-hydroxyvitamin D₃ status and pregnancy outcome. *Int J Gynaecol Obstet* 2012; 116: 6–9.
- [16] Shin JS, Choi MY, Longtine MS, Nelson DM. Vitamin D effects on pregnancy and the placenta. *Placenta* 2010; 31: 1027–1034.
- [17] Hashemipour S, Ziaee A, Javadi A, Movahed F, Elmizadeh K, Javadi EH, et al. Effect of treatment of vitamin D deficiency and insufficiency during pregnancy on fetal growth indices and maternal weight gain: a randomized clinical trial. *Eur J Obstet Gynecol Reprod Biol* 2014; 172: 15.
- [18] Clifton-Bligh RJ, McElduff P, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. *Diabet Med* 2008; 25: 678–684.
- [19] Soheilykhah S, Mojibian M, Rashidi M, Rahimi-Saghand S, Jafari F. Maternal vitamin D status in gestational diabetes mellitus. *Nutr Clin Pract* 2010; 25: 524–527.
- [20] Karhapää P, Pihlajamäki J, Pörsti I, Kastarinen M, Mustonen J, Niemelä O, et al. Diverse associations of 25-hydroxyvitamin D and 1, 25-dihydroxy-vitamin D with dyslipidaemias. *J Intern Med* 2010; 268: 604–610.
- [21] Al-Ajlan A, Krishnaswamy S, Alokail MS, Aljohani NJ, Al-Serehi A, Sheshah E, et al. Vitamin D deficiency and dyslipidemia in early pregnancy. *BMC Pregnancy ChildB* 2015; 15: 314.
- [22] Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. *Am J Clin Nutr* 2004; 79: 820–825.
- [23] Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF. Association between vitamin D deficiency and primary cesarean section. *J Clin Endocrinol Metab* 2009; 94: 940–945.
- [24] Hollis BW, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: double-blind, randomized clinical trial of safety and effectiveness. *J Bone Miner Res* 2011; 26: 2341–2357.
- [25] Holick MF. Vitamin D: the other steroid hormone for muscle function and strength. *Menopause* 2009; 16: 1077–1078.